Remarks

By the foregoing Amendment, Claim 1 is amended. Entry of the Amendment and favorable consideration thereof is earnestly requested.

Applicant would like to thank the Examiner for withdrawing objections to the abstract, specification, as well as the objections under 35 U.S.C. 112 made in the office action mailed 11/17/2003.

The Examiner has maintained an objection to the specification for containing abbreviations on page 34, line 17 of the specification, namely "MLN" and "CLN". The applicant respectfully submits that the specification was clear, however, has amended the specification to include full words for clarity as suggested by the Examiner. Thus the objection is moot.

The Examiner has maintained the rejection of Claim 1 as being anticipated by Holmgren (5,681,571). Applicant respectfully asks the Examiner to reconsider the rejection in view of the above Amendments and the below Remarks.

Amended claim 1 requires, among other limitations, administering to the subject an effective amount of the B subunit of E. Coli. heat labile enterotoxin (EtxB), wherein the EtxB is free from whole toxin and not linked to an antigen. Nowhere does Holmgren disclose administering to the subject an effective amount of the B subunit of E. Coli. heat labile enterotoxin (EtxB), wherein the EtxB is free from whole toxin and not linked to an antigen. Accordingly, claim 1 is not anticipated by Holmgren. Reconsideration is urged.

Moreover Holmgren does not make the claimed invention obvious. One of ordinary skill in the art would not have been motivated to adapt Holmgren to require EtxB to be free from whole toxin and not linked to an antigen. This is especially true since Holmgren teaches away from the claimed invention by requiring that the specific tolero-

gen to be linked to a mucosa-binding molecule. Thus, it is more likely that one of ordinary skill in the art would have been motivated by Holmgren to link EtxB with some other protein, rather than require that it not be linked to an antigen as required by the claimed invention. Thus, claim 1 is not obvious.

The Examiner has rejected Claims 1, 3, 4, and 5 as obvious over Clements (6,413,523) in light of Marcello *et al.* (of record). Reconsideration is urged in light of the remarks below.

Clements relates to the whole toxin of E. Coli. (LT), and not LTB (EtxB) which is the B subunit of the whole toxin. In fact, it is specifically stated in Clements that the B subunit of the whole toxin did not work. *See* column 8, lines 2-5. Thus, EtxB is not shown to be involved in influencing the immune system, and a person of ordinary skill in the art would be taught away from using EtxB to boost the immune response to a vaccine according to the present invention.

Marcello relates to mimetic peptides capable of selectively disrupting protein-protein interactions representing potential therapeutic agents for inhibition of viral or cellular enzymes. The B subunit of *E. Coli.* heat-labile enterotoxin can be used as a recombinant carrier for the receptor-mediated delivery of YAGAVVNDL into virally infected cells. The nonapeptide has an inherent antiviral activity which is completely out with any effect on the immune system. It was concluded that the activity of EtxB-R2 depends on the covalently linked nonapeptide. Indeed, the data provided by Marcello was produced in an *in vitro* system that does not contain any cells of the immune system, showing that the anti-viral effect is not a result of any enhancement of immune response.

Amended claim 1, requires, among other limitations, administering to the subject an effective amount of the B subunit of *E. Coli.* heat labile enterotoxin (EtxB), wherein the EtxB is free from whole toxin and not linked to an antigen. Neither reference, either

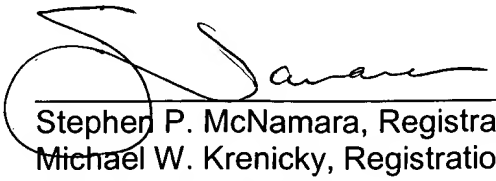
alone, or in combination, discloses using an effective amount of EtxB which is :1) free from whole toxin; and 2) not linked to an antigen. Thus, the references, taken alone or in combination, fail to makes claim 1 obvious.

Furthermore, one of ordinary skill in the art would not be motivated to modify LT disclosed in Clements with the mimetic peptides of Marcello in order to administer effective amounts of EtxB, free from whole toxin, and not linked to an antigen in order to enhance the level of immune response to a vaccine against an infectious agent. Clements teaches away from the claimed invention by stating that the B subunit alone was unable to influence tolerance induction. Marcello does not even relate to an effect on the immune system. Thus, there is no motivation to combine the references, and claim 1 is not obvious.

Moreover, even if one did combine the references, it is likely that one of ordinary skill in the art would arrive at using whole toxin linked to a peptide for drug delivery and not the use of EtxB, free from whole toxin and not linked to an antigen to boost the immune response. Claim 1 is not obvious.

For the foregoing reasons, Applicant respectfully submits that all Claims 1, 3, 4, 5 are patentable over the references of record, and earnestly solicits allowance of the same.

Respectfully submitted,



Stephen P. McNamara, Registration No. 32,745
Michael W. Krenicky, Registration No. 45,411
Attorneys for Applicants
ST.ONGE STEWARD JOHNSTON & REENS LLC
986 Bedford Street
Stamford, CT 06905-5619
203 324-6155